Please amend the subject application as follows:

In the specification:

Please amend the title at page 1, lines 3- 4 as follows:

-- METHODS OF INDUCING ORGAN TRANSPLANT TOLERANCE AND CORRECTING HEMOGLOBINOPATHIES USING L104EA29YIg IN CONJUNCTION WITH AN ALKYLATING AGENT --

Please amend the specification at page 30, lines 1-7 as follows:

-- In addition, other immunosuppresive agents can be used in the methods of the invention. Examples include: cyclosporin, azathioprine, methotrexate, lymphocyte immune globulin, anti-CD3 antibodies, Rho (D) immune globulin, adrenocorticosteroids, sulfasalzine, FK-506. methoxsalen, mycophenolate mofetil (CELLCEPT®), horse anti-human thymocyte globulin (ATGAM®), humanized anti-TAC (HAT), basiliximab (SIMULECT®), rabbit anti-human thymocyte globulin (THYMOGLOBULIN®), sirolimus or thalidomide. --

Please amend the specification at page 45, lines 1-7 as follows:

-- **Flow cytometric analysis.** Peripheral blood was analyzed by staining with fluorochrome-conjugated antibodies (anti-CD3, anti-CD5, anti-CD11b, anti-GR1, anti-B220, anti-H-2K^{d}, anti-H-2K^{b}, anti-Vβ11, anti-Vβ5.1/5.2, anti-Vβ8.1/8.2 (Pharmingen), anti-CD4, anti-CD8 (Caltag Laboratories, Burlingame, CA), or immunoglobulin isotype controls (Pharmingen)), followed by red blood cell lysis and washing with a whole blood

lysis kit (R+D Systems, Minneapolis, MN). Stained cells were analyzed using Cellquest software on a FACSCalibur™ flow cytometer (Becton Dickinson, Mountain View, CA).

Please amend the specification at page 58, lines 12-21 as follows:

-- Recipient mice received 2 x 10^7 BALB/c, T-cell depleted (with anti-CD3, anti-CD4, anti-CD8 antibodies, Miltenyi Inc., Auburn, CA) bone marrow (TDBM) on day 0, as described above, BUSULFEX® (busulfan 20mg/kg, i.p., Orphan Medical, Minnetonka, MN) on day -1, and 500 μg of hamster anti-mouse-CD40L mAb (MR1, BioExpress, Lebanon, NH) and 500 μg human CTLA4-Ig (Bristol-Myers Squibb, Princeton, NJ), (for costimulation blockade) i.p. on days 0, 2, 4, 6 relative to the bone marrow transplant. Control mice received costimulation blockade and T cell depleted bone marrow, but no busulfan. The base-line hematological parameters were measured one week prior to transplant, and chimerism was tested two weeks, four weeks, and at monthly intervals after transplant. --

Please amend the specification at page 59, lines 7-14 as follows:

-- Complete Blood Counts were performed on a HEMAVET® 1500 blood analyzer (1500 R series, CDC technologies, Oxford, CT). Reticulocyte counts were performed by flow cytometry of peripheral blood labeled with antibodies specific for red blood cells (anti-Ter-119, Pharmingen) and white blood cells (anti-CD45, Pharmingen) and a fluorescent label of RNA, Thiazole-Orange (Sigma Inc., St. Louis, MO). Reticulocyte counts were defined as the percent of peripheral blood cells that were Ter-119-Positive, Thiazole-Orange-positive, and CD45-negative. "Stress" reticulocytes were also analyzed by labeling with an antibody against the transferrin receptor (CD71, Pharmingen). --

Please amend the specification at page 69, lines 25-31 through page 70, lines 1-5 as follows:

-- Specifically, single-site mutant nucleotide sequences were generated using non-mutated (e.g., wild-type) DNA encoding CTLA4Ig (U.S. Patent Nos: 5,434,131, 5,844,095; 5,851,795; and 5,885,796; ATCC Accession No. 68629) as a template. Mutagenic oligonucleotide PCR primers were designed for random mutagenesis of a specific codon by allowing any base at positions 1 and 2 of the codon, but only guanine or thymine at position 3 (XXG/T or also noted as NNG/T). In this manner, a specific codon encoding an amino acid could be randomly mutated to code for each of the 20 amino acids. In that regard, XXG/T mutagenesis yields 32 potential codons encoding each of the 20 amino acids. PCR products encoding mutations in close proximity to the CDR3-like loop of CTLA4Ig (MYPPPY (SEQ ID NO:15)), were digested with SacI/XbaI and subcloned into similarly cut CTLA4Ig (as included in Figure 20) πLN expression vector. This method was used to generate the single-site CTLA4 mutant molecule L104EIg (as included in Figure 14). --

Please amend the specification at page 69, lines 25-31 through page 70, lines 1-5 as follows:

-- The solution structure of the extracellular IgV-like domain of CTLA4 has recently been determined by NMR spectroscopy (Metzler et al., (1997) Nature Struct. Biol., 4:527-531). This allowed accurate location of leucine 104 and alanine 29 in the three dimensional fold (Figure 22 left and right depictions). Leucine 104 is situated near the highly conserved MYPPPY amino acid sequence (SEQ ID NO:15). Alanine 29 is situated near the C-terminal end of the CDR-1 (S25-R33) region, which is spatially adjacent to the MYPPPY region (SEQ ID NO:15). While there is significant interaction between residues at the base of these two regions, there is apparently no direct interaction

between L104 and A29 although they both comprise part of a contiguous hydrophobic core in the protein. The structural consequences of the two avidity enhancing mutants were assessed by modeling. The A29Y mutation can be easily accommodated in the cleft between the CDR-1 (S25-R33) region and the MYPPPY region (SEQ ID NO:15), and may serve to stabilize the conformation of the MYPPPY region (SEQ ID NO:15). In wild type CTLA4, L104 forms extensive hydrophobic interactions with L96 and V94 near the MYPPPY region (SEQ ID NO:15). It is highly unlikely that the glutamic acid mutation adopts a conformation similar to that of L104 for two reasons. First, there is insufficient space to accommodate the longer glutamic acid side chain in the structure without significant perturbation to the CDR-1 (S25-R33 region). Second, the energetic costs of burying the negative charge of the glutamic acid side chain in the hydrophobic region would be large. Instead, modeling studies predict that the glutamic acid side chain flips out on to the surface where its charge can be stabilized by solvation. Such a conformational change can easily be accommodated by G105, with minimal distortion to other residues in the regions. --

Please amend the specification at page 72, lines 4-13 as follows:

-- COS cells were transfected with individual miniprep purified plasmid DNA and propagated for several days. Three day conditioned culture media was applied to BIAcore™ biosensor chips (Pharmacia Biotech AB, Uppsala, Sweden) coated with soluble CD80Ig or CD86Ig. The specific binding and dissociation of mutant proteins was measured by surface plasmon resonance (O'Shannessy, D. J., et al., 1997 *Anal. Biochem.* 212:457-468). All experiments were run on BIAcore™ or BIAcore™ 2000 biosensors at 25°C. Ligands were immobilized on research grade NCM5 sensor chips (Pharmacia) using standard N-ethyl-N'-(dimethylaminopropyl) carbodiimidN-hydroxysuccinimide coupling (Johnsson, B., et al. (1991) Anal. Biochem. 198: 268-277; Khilko, S.N., et al.(1993) J. Biol. Chem 268:5425-15434). --

Please amend the abstract at page 120, lines 8-11 as follows:

-- Methods of establishing hematopoietic chimerism ~~useful to correct hematological diseases and promote acceptance of organ transplants include administering busulfan, costimulation blockade, and readily attainable numbers of T cell depleted bone marrow cells.~~ and inhibiting solid organ or tissue/cellular transplant rejection include administering T cell depleted bone marrow before, during or after solid organ or tissue/cellular transplant, subsequently administering busulfan in an amount that facilitates mixed chimerism, and administering an immunosuppressive composition that blocks T cell costimulatory signals before, during and after transplant. --